Mapping insomnia

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Chapter 2

Scope of the present thesis

The current study was firstly performed to characterize how insomnia patients can be discriminated from people without sleep complaints with respect to behavior, brain function and brain structure. If differences exist, it is of importance to establish whether they represent risk factors that could have been present already before the onset of insomnia, or rather represent consequences of insomnia, i.e. induced by this chronic condition. We therefore planned our studies to allow for conclusions on inducibility and reversibility of possible differences. Thus, we evaluated the inducibility of effects by assessing subjects without sleep complaints both before and after enforcing the shallow sleep that is typical of insomnia, and we evaluated the reversibility of possible insomnia effects by assessing insomniacs both before and after treating them with non-pharmacological sleep therapy.

For two reasons, we focused on older adults, between 50 and 75 years of age. First, the prevalence of insomnia strongly increases with age[4], making it the most relevant group to study. Second, we noticed that both experimental sleep deprivation and normal aging are associated most prominently with changes in prefrontal function. This observation, in combination with the age-related increase in sleep problems, led us to question to what extent sleep problems add to what is commonly referred to as 'age-related cognitive decline'. In other words: to what extent might this reflect 'poor-sleep-induced cognitive decline'?

To investigate whether the possible differences between insomnia patients and controls without sleep complaints normalize after well established non-pharmacological sleep therapy, CBT supported by chronobiological treatment was applied for 6 weeks, after which all assessments were performed once more. The group of controls without sleep complaints received selective slow wave suppression during two nights, either on their first or second session, which was randomly divided over participants.

On the basis of the current neuroimaging literature on sleep disruption, we expected to find prefrontal hypoactivation in insomnia, with compensatory activation in non-task related regions. We expected normalization of activation levels after sleep therapy, both on hypoactivation and on compensatory activation. On the basis of previous findings, we expected temporal and prefrontal regions to show less grey and white matter in insomnia patients compared to controls. We also expected the behavioral and brain activation outcomes of experimental selective slow wave suppression to be qualitatively comparable to insomnia findings, albeit possibly less strong.

In this thesis, we will try to answer the following questions:

- Given the equivocal neuropsychological test results of previous work, yet the pronounced subjective complaints, would it be possible to find insomnia-

related performance differences on computerized tasks with high resolution reaction time sampling and subtle changes in task parameters?

- **Chapter 3** will focus on such a behavioral correlate of chronic insomnia, by measuring a simple and slightly more complex vigilance task before and after sleep therapy or waitlist control.
- What are the brain activation patterns in older insomniacs performing two verbal fluency tasks that differ in complexity? If brain activation patterns differ from those of controls, can non-pharmacological sleep therapy normalize them? **Chapter 4** discusses how chronic insomnia patients differ from age-matched controls with respect to performance and brain activation on two verbal fluency tasks, and whether differences normalize after sleep therapy.
- **Chapter 5** discusses structural brain correlates of chronic insomnia. Are there volumetric grey or white matter differences between chronic insomnia patients and age-matched controls? And if so, are they truly related to sleep complaints or rather confounds of factors like depression or age, that are known to affect regional brain volume?
- Further 'state' factors of insomnia are discussed in **Chapter 6**, where the effects of double pulse transcranial magnetic stimulation are compared between groups and before and after sleep therapy. TMS was applied to test the hypothesis of changes in the balance between GABA-ergic inhibitory and glutamatergic excitatory neurons in cortical networks[61]. Do insomnia patients show normal levels of intracortical facilitation, normally induced by double pulse TMS?
- Insomnia is known to be related to reduced slow wave sleep. To investigate the comparability between insomnia and experimentally induced shallow sleep, slow wave suppression was applied in older adults without sleep complaints, who performed the same tasks as insomnia patients. In **Chapter 7**, the performance on vigilance tasks is discussed before and after slow wave suppression.
- **Chapter 8** discusses how selective slow wave suppression in normal sleeping controls not only affects memory performance but also affects hippocampal brain activation. The data are compared to similar findings after total sleep deprivation.

The general discussion in **Chapter 9** will integrate the findings to answer the questions whether insomnia is or is not characterized by alterations in performance and brain activation and whether these are reversible consequences of insomnia or rather irreversible possible risk factors for developing insomnia. This chapter includes a discussion on how our findings suggest directions for future research to reach a better understanding of the condition of chronic insomnia.

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